Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1 (currently amended). A method for treatment or prophylaxis of disease caused by deficiency, in a human subject, of ~~an~~ a human enzyme belonging to the heme biosynthetic pathway, the method comprising administering, to the subject, an effective amount of ~~a catalyst which is~~ said enzyme, ~~or an enzymatically equivalent fragment or analogue thereof~~
wherein the disease is selected from the group consisting of acute intermittent porphyria (AIP), ALA deficiency porphyria (ADP), Porphyria cutanea tarda (PCT), Hereditary coproporphyria (HCP), Harderoporphyria (HDP), Variegata porphyria (VP), Congenital erythropoetic porphyria (CEP), Erythropoietic protoporphyria (EPP), Hepatoerythropoietic porphyria (HEP), and

when the disease is Acute intermittent porphyria (AIP), the enzyme is Phorbilinogen deaminase (PBGD),
when the disease is ALA deficiency porphyria (ADP), the enzyme is ALA dehydratase,
when the disease is Porphyria cutanea tarda (PCT), the enzyme is Uroporphyrinogen decarboxylase,
when the disease is Hereditary coproporphyria (HCP), the enzyme is Coproporphyrinogen oxidase,
when the disease is Harderoporphyria (HCP), the enzyme is Coproporphyrinogen oxidase,
when the disease is Variegata porphyria (VP), the enzyme is Protoporphyrinogen oxidase,
when the disease is Congenital erythropoetic porphyria (CEP), the enzyme is Uroporphyrinogen III synthase,
when the disease is Erythropoietic protoporphyria (EPP), the enzyme is Ferrochelatase, and
when the disease is Hepatoerythropoietic porphyria (HEP), the

enzyme is Uroporphyrinogen decarboxylase.

2-3 (cancelled).

4 (currently amended). A method according to claim 1, wherein the disease is AIP and the enzyme is PBGD ~~or an enzymatically equivalent fragment or analogue thereof~~.

5 (currently amended). A method according to claim 1, wherein the enzyme ~~catalyst~~ is a recombinantally produced ~~form of the~~ enzyme ~~belonging to the heme biosynthetic pathway or of the enzymatically equivalent fragment or analogue thereof~~.

6 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is administered by a route selected from the group consisting of the intravenous route, the intraarterial route, the intracutaneous route, the subcutaneous route, the oral route, the buccal route, the intramuscular route, the anal route, the transdermic route, the intradermal route, and the intratechal route.

7 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is formulated in an isotonic solution.

8 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is lyophilised.

9 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is sterile filtered.

10 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is formulated as lipid vesicles comprising phosphatidylcholine or phosphatidylethanolamine or combinations thereof.

11 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is incorporated into erythrocyte ghosts.

12 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is formulated as a sustained release formulation comprising biodegradable microspheres.

13 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is lyophilized in a two-compartment

cartridge, where the ~~catalyst~~ enzyme will be in the front compartment and water for reconstitution in the rear compartment.

14 (currently amended). A method according to claim 13, wherein the two compartment cartridge is combined with an injection device to administer the ~~catalyst~~ enzyme either by a needle or by a needle-less (high pressure) device.

15 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is formulated in a physiological buffer containing an enhancer for nasal administration.

16 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is formulated as an oral formulation containing lipid vesicles.

17 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is formulated so as to enhance the half-life thereof in the subject's bloodstream.

18 (currently amended). A method according to claim 17, wherein the ~~catalyst~~ enzyme has a polyethylene glycol coating.

19 (currently amended). A method according to claim 17, wherein the ~~catalyst~~ enzyme is complexed with a heavy metal.

20-22 (cancelled).

23 (currently amended). A method according to claim ~~22~~ 1, wherein the ~~catalyst~~ enzyme is tagged with a ligand specifically recognized by a liver cell whereby the tagged molecule is internalized by the liver cell.

24 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme exerts substantially all its enzymatic activity extracellularly in the bloodstream.

25 (cancelled).

26 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme has been prepared by a method comprising

a) introducing, into a suitable vector, a nucleic acid fragment which includes a nucleic acid sequence encoding the ~~catalyst~~ enzyme;

b) transforming a compatible host cell with the vector;
c) culturing the transformed host cell under conditions facilitating expression of the nucleic acid sequence; and
d) recovering the expression product from the culture and optionally subjecting the expression product to post-translational processing, ~~such as in vitro protein refolding, enzymatic removal of fusion partner, alkylation of amino acid residues, and deglycosylation,~~ so as to obtain the ~~catalyst~~ enzyme.

27 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme has been prepared by liquid-phase or solid-phase peptide synthesis.

28 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is free from any other biological material of human origin.

29 (currently amended). A method according to claim 1, wherein the ~~catalyst~~ enzyme is administered at least once a day.

30 (previously presented). A method according to claim 1, wherein the daily dosage is in the range of 0.01-1.0 mg/kg body weight per day.

31 (previously presented). A method according to claim 1, wherein the daily dosage is about 0.1 mg per kg body weight per day.

32-35 (cancelled).

36 (currently amended). A method according to claim 1 wherein the ~~catalyst~~ enzyme is recombinant human PBGD encoded by ~~based on any of~~ Seq. ID NO 1 (clone PBGD 1.1) ~~and~~ or Seq. ID NO 12 (non-erythro PBGD 1.1.1).

37 (currently amended). A pharmaceutical composition comprising ~~catalyst according to claim 32, which is~~ recombinant human PBGD ~~based on any of~~ encoded by Seq. ID NO 1 (clone PBGD 1.1) ~~and~~ or Seq. ID NO 12 (non-erythro PBGD 1.1.1).

38 (withdrawn, currently amended). A method for treating a patient having a mutation in the PBGD gene causing an enzyme defect, comprising the use of a human PBGD cDNA sequence of

either non-erythropoietic form or erythropoietic form according to the tissue in which PBGD should be expressed, and transfection of the patient with the relevant cDNA.

39 (withdrawn; currently amended). The method according to claim 38 wherein the enzyme deficiency ~~defiency~~ is selected from enzyme deficiencies ~~defiencies~~ resulting in a disease selected from the group consisting of Acute Intermittent Porphyria[[,]] (AIP), ALA deficiency porphyria (ADP), Porphyria cutanea tarda (PCT), Hereditary coproporphyria (HCP), Harderoporphyria (HDP), Variegated porphyria (VP), Congenital erythropoietic porphyria (CEP), Erythropoietic protoporphyria (EPP), and Hepatoerythropoietic porphyria (HEP).

40 (withdrawn; currently amended). The method according to claim 39 wherein the disease is Acute Intermittent Porphyria~~, (AIP)~~.

41 (withdrawn; currently amended). The method according to claim 38 wherein the human PBGD cDNA sequence is ~~selected from~~ Seq. ID NO 1 (clone PBGD 1.1) ~~and~~ or Seq. ID NO 12 (non-erythro PBGD 1.1.1).

42 (withdrawn). The method according to claim 38 wherein the transfection is by use of a vector selected from the group consisting of adenovirus, retrovirus and associated adenovirus.

43 (withdrawn). The method according to claim 38 wherein the PBGD gene transfer vector into human cells (erythropoeitic and/or non-erythropoietic) results in normal PBGD activity.

44 (withdrawn). A method of gene therapy treatment of patients with Acute Intermittent Porphyria (AIP) comprising correction of one of the specific point mutations identified causing AIP by use of chimeraplasty gene repair.

45 (withdrawn; currently amended). The method according to claim 43 wherein said correction is effected by transfection with a delivery system which delivers a corrected gene, and wherein the delivery system for transfection is by use of non-viral vectors formulated in a vehicle preparation comprising one or more components selected from the group consisting of cationic

phospholipids, phospholipids, phospholipids mixed with neutral lipids, lictosylated PEI, and liposomes ~~liposomes comprising mixtures of natural phospholipids and neutral lipids~~.

46 (withdrawn; currently amended). A method according to claim 44 wherein the mutation is selected from the list of mutations in Table A.

47 (cancelled).

48. The method of claim 1 in which the disease is AIP and the enzyme is PBGD ~~or an enzymatically equivalent fragment or mutant thereof~~.

49-51 (cancelled).